

CLAIMS

1. A compound having affinity with a calcified tissue represented by the formula: $(AC)_a-MC-(LI)_b$ wherein MC is a mother nucleus and represents a residue
5 of a compound having a plurality of functional groups selected from the group consisting of an amino group, an amide group, a hydroxyl group, a thiol group, a thioether group, a sulfonyl group, a phosphonyl group, an aldehyde group, a carboxyl group, a carbonyl group, a halogen, and
10 a cyano group;
AC is a group having affinity with a calcified tissue;
LI is a ligand for binding to a metal atom; and
a is an integer of 1 or more, and b is 0 or an integer of 1 or more.
- 15 2. The compound having affinity with a calcified tissue according to claim 1, wherein the mother nucleus MC is a residue of a compound selected from the group consisting of a monosaccharide, an oligosaccharide, an amino oligosaccharide, a cyclodextrin and a saccharide
20 dendrimer.
3. The compound having affinity with a calcified tissue according to claim 1 or 2, wherein the AC is selected from the group consisting of polyaspartic acid, polyglutamic acid and organic phosphonic acid.
- 25 4. The compound having affinity with a calcified tissue according to claim 1, wherein the mother nucleus MC is a residue of a compound selected from the group consisting

of an oligosaccharide, an amino oligosaccharide, a cyclodextrin and a saccharide dendrimer, and the group AC having affinity with a calcified tissue is bonded to a constituent monosaccharide of the mother nucleus MC, and
5 the ligand LI for binding to a metal atom is bonded to a constituent monosaccharide other than the above-mentioned constituent monosaccharide.

5. The compound having affinity with a calcified tissue according to claim 4, wherein a plurality of the groups
10 AC having affinity with a calcified tissue or a plurality of the ligands LI for binding to a metal atom are bonded to the mother nucleus MC.

6. The compound having affinity with a calcified tissue according to any one of claims 1 to 5, wherein at least
15 one of the mother nucleus MC, the group AC having affinity with a calcified tissue and the ligand LI contains a metal atom or an isotope of a halogen atom, carbon, oxygen, nitrogen, sulfur or phosphorus.

7. The compound having affinity with a calcified tissue
20 according to any one of claims 1 to 6, which forms a complex with a metal atom.

8. The compound having affinity with a calcified tissue according to any one of claims 1 to 7, wherein the mother nucleus MC is a residue of a linear or branched
25 oligosaccharide of 2 to 20 saccharide units which comprises a constituent monosaccharide selected from the group consisting of glucose, mannose and galactose.

9. The compound having affinity with a calcified tissue according to any one of claims 1 to 7, wherein the mother nucleus MC is a residue of a linear or branched amino oligosaccharide of 2 to 20 saccharide units which
- 5 comprises a constituent monosaccharide selected from the group consisting of glucosamine, mannosamine and galactosamine.
10. The compound having affinity with a calcified tissue according to claim 9, wherein a part of the amino
- 10 oligosaccharide that constitutes the mother nucleus MC is reduced.
11. The compound having affinity with a calcified tissue according to claim 9, wherein a part of the amino oligosaccharide that constitutes the mother nucleus MC is
- 15 N-acetylated.
12. The compound having affinity with a calcified tissue according to any one of claims 8 to 11, wherein the oligosaccharide or amino oligosaccharide comprises constituent monosaccharides that are α - or β -linked.
- 20 13. The compound having affinity with a calcified tissue according to any one of claims 8 to 11, wherein the oligosaccharide or amino oligosaccharide comprises constituent monosaccharides that are 1-3, 1-4 or 1-6-linked.
- 25 14. The compound having affinity with a calcified tissue according to any one of claims 1 to 7, wherein the mother

nucleus MC comprises a residue of a cyclodextrin selected from the group consisting of α -, β - and γ -cyclodextrins.

15. The compound having affinity with a calcified tissue according to claim 14, wherein the cyclodextrin is a

5 dialdehyde saccharide which comprises a constituent monosaccharide that is reduced at positions 2 and 3.

16. The compound having affinity with a calcified tissue according to any one of claims 1 to 7, wherein the mother nucleus MC comprises a residue of a saccharide dendrimer,

10 and the saccharide dendrimer comprises a linear or branched saccharide bonded to a core comprising a polycarboxylic acid or an alkyl polycarboxylic acid.

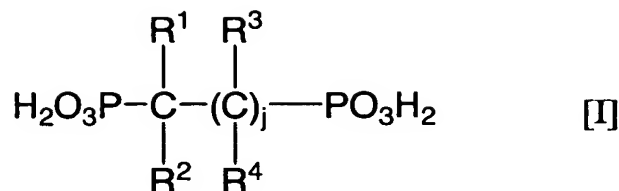
17. The compound having affinity with a calcified tissue according to any one of claims 1 to 7, wherein the mother

15 nucleus MC comprises a residue of a saccharide dendrimer, and the saccharide dendrimer comprises a linear or branched saccharide bonded to a core comprising a polyamine or an alkylpolyamine.

18. The compound having affinity with a calcified tissue

20 according to any one of claims 1 to 17, wherein the group AC having affinity with a calcified tissue comprises an organic phosphonic acid, and the organic phosphonic acid is a residue of a diphosphonic acid represented by the following formula I, derivatives thereof or salts

25 thereof:



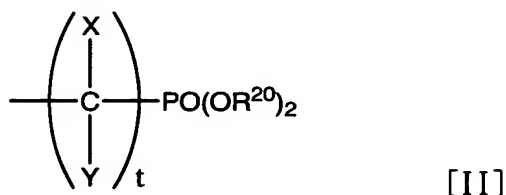
(wherein,

R^1 and R^3 , which are the same or different, each represents a formula $-(\text{CR}^5\text{R}^6)_k-\text{R}^7_1-(\text{CR}^8\text{R}^9)_m-\text{R}^{10}_n-(\text{CR}^{11}\text{R}^{12})_o-$
5 $\text{R}^{13}_p-(\text{CR}^{14}\text{R}^{15})_q\text{R}^{16}$ (wherein R^5 , R^6 , R^8 , R^9 , R^{11} , R^{12} , R^{14} , R^{15} and R^{16} are groups each independently selected from the group consisting of H, -OH, -COOH, -C(NH₂)=NH, -CN, -SO₃H, -NR¹⁷₂ and a halogen atom, R^{17} is independently H or -
(CH₂)_rCH₃ respectively, R^7 , R^{10} and R^{13} are groups each
10 independently selected from the group consisting of sulfur, oxygen, amide, imide, a divalent heterocycle consisting of 3 to 12 atoms and a cyclic hydrocarbon (Ar($\text{R}^{18}_r-\text{R}^{19}_s$)), R^{18} is -CR⁵R¹⁷, R^{19} is independently selected from the group consisting of H, -OH, -COOH, -
15 C(NH₂)=NH, -CN, -SO₃H, -NH₂, -NHMe, -NMe₂ and a halogen atom; k, l, m, n, o, p and q are each independently 0 or an integer of 1 or more, r is 0 to 3, s is 0 to 12, and the sum total of k, l, m, n, o, p and q is 0 to 12);
 R^2 is a group selected from H, -OH, -NH₂, -NHMe, -NMe₂, -
20 CN, and a lower alkyl group (which may be substituted with one or a plurality of polar groups);
 R^4 is a group selected from H, -OH, -NH₂, -NHMe, -NMe₂, -CN, -SO₃H, a halogen and a lower alkyl group (which may

be substituted with one or a plurality of polar groups);
and

j is 0 or 1 (provided that, when j is 0, R¹ is not H and when j is 1, both of R¹ and R³ cannot be H).

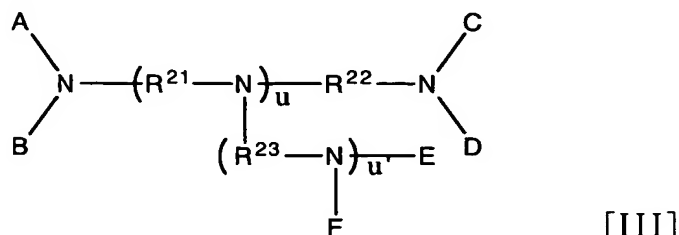
- 5 19. The compound having affinity with a calcified tissue according to any one of claims 1 to 17, wherein the group AC having affinity with a calcified tissue comprises an organic phosphonic acid, and the organic phosphonic acid is an organic aminophosphonic acid derivative having an
10 amine nitrogen atom to which a group represented by the formula II is bonded, or an ester or a salt thereof:



- (wherein t is an integer of 1 to 8; X and Y are each
15 independently selected from hydrogen, a halogen group, a hydroxyl group, a carboxyl group, a carbonyl group, a phosphonic acid group, and a hydrocarbon group having 1 to 8 carbon atoms, and when t is larger than 1, each X and Y may be the same or different; R²⁰ is selected from
20 hydrogen, a silyl group, an alkyl group, a benzyl group, sodium and potassium).

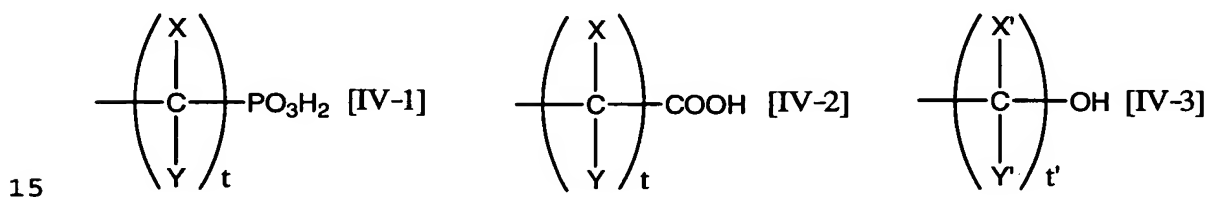
20. The compound having affinity with a calcified tissue according to any one of claims 1 to 17, wherein the group AC having affinity with a calcified tissue comprises an

organic phosphonic acid, and the organic phosphonic acid is a phosphonic acid derivative represented by the formula III, an ester or a salt thereof.



5

(wherein each u and u' is independently an integer of 0 to 5, preferably 0, 1, or 2; R²¹, R²² and R²³ are each independently -(CH₂)_v- (v= 1 to 5); A, B, C, D, E, and F are each independently selected from the group consisting of hydrogen, a methyl group, an ethyl group, an isopropyl group, a pivaloyl group, a benzyl group, an acetyl group, a trifluoroacetyl group, and groups of the following formulae IV-1 to 3, and one of A, B, C, D, E and F is the group of following formula IV-1.



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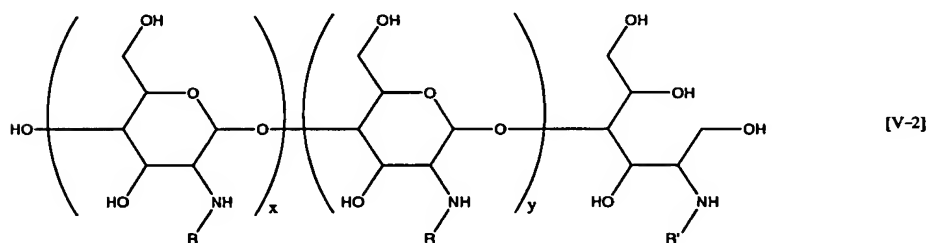
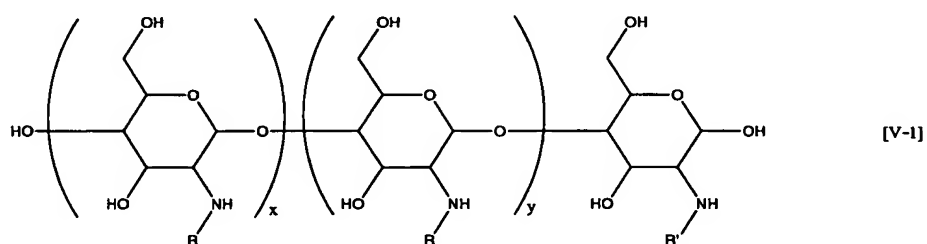
(wherein t, X and Y are the same as in the above-mentioned formula II; t' is 2 or 3; X' and Y' are each independently selected from hydrogen, a methyl group and an ethyl group, and each X' and Y' may be the same or different)).

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21. The compound having affinity with a calcified tissue according to any one of claims 1 to 20, wherein the ligand (LI) for binding to a metal atom has a coordinating atom selected from oxygen, sulfur, phosphorus, nitrogen and carbon.
22. The compound having affinity with a calcified tissue according to any one of claims 1 to 20, wherein the ligand (LI) for binding to a metal atom is selected from the group consisting of ethylenediaminetetraacetic acid (EDTA), diethylenetriaminepentaacetic acid (DTPA), triethylenetetraaminehexaacetic acid (TTHA), cyclam, 1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid (TETA), 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA), N{1-2,3-dioleyloxy}propyl}-N,N,N-triethylammonium (DOTMA), mercaptoacetylglucylglycine (MAG3), ethylene cysteine dimer (ECD), hydrazinonicotinyl (HYNIC), lysine-tyrosine-cysteine (KYC), cysteine-glycine-cysteine (CYC), N,N'-bis(mercaptoacetamide)ethylenediamine (DADS), N,N'-bis(mercaptoacetamide)-2,3-diamine propanoic acid (CO2DADS), N,N'-bis(2-mercaptoethyl)ethylenediamine (BATs), thiosemicarbazone, propylene amineoxime (PnAO), and other amineoxime ligands and derivatives thereof.
23. The compound having affinity with a calcified tissue according to any one of claims 1 to 21, wherein the AC or LI has a linker L through which the AC or LI is coupled with the mother nucleus MC.

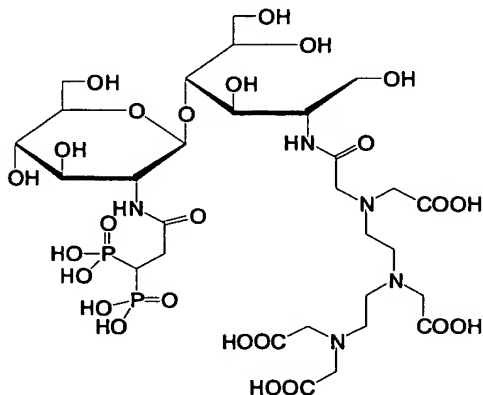
24. The compound having affinity with a calcified tissue according to claim 22, wherein the linker L is selected from the group consisting of peptide, alkyl, and alkyl ether, alkylamide, alkylamine and alkylolefin represented by formula $-(CH_2)_w-R^{24}-(CH_2)_w-$ (wherein w is each independently 0 to 5, and R^{24} is O, S, NHCO, NH, or CH=CH).

25. The compound having affinity with a calcified tissue according to claim 1, which is represented by the following formula V-1 or V-2:



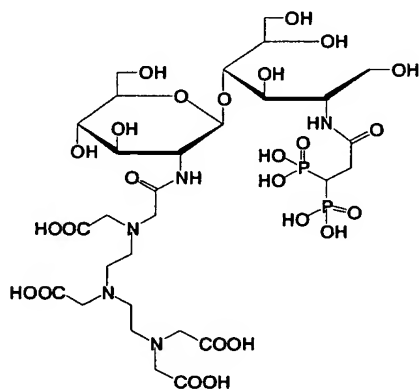
(wherein R and R' are each independently a group AC having affinity with a calcified tissue or a ligand LI for binding to a metal atom, and at least one of them is the group AC having affinity with a calcified tissue; x and y are each independently 0 to 19; and x+y is 1 to 19).

26. The compound having affinity with a calcified tissue, represented by the following formula VI-1:



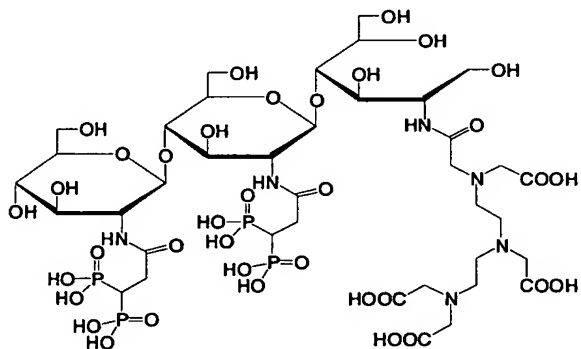
[VI-1]

27. The compound having affinity with a calcified tissue, represented by the following formula VI-2:



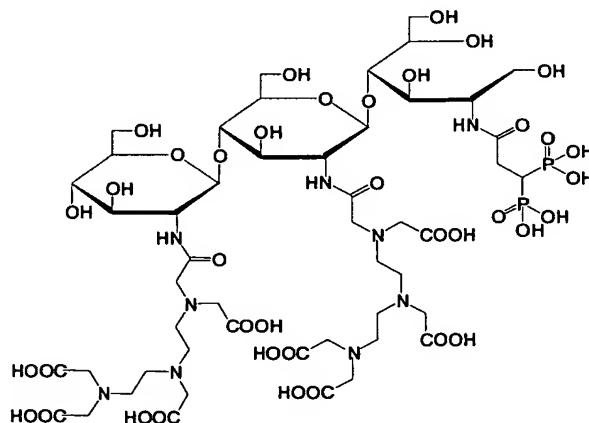
[VI-2]

28. The compound having affinity with a calcified tissue, represented by the following formula VII-1:



[VII-1]

29. The compound having affinity with a calcified tissue, represented by the following formula VII-2:



[VII-2]

30. The compound having affinity with a calcified tissue according to any one of claims 25 to 29, which forms a complex with a metal atom.

31. The compound having affinity with a calcified tissue according to any one of claims 1 to 30, wherein the metal atom which forms a complex or a metal atom or isotope element contained in the mother nucleus MC, the group AC having affinity with a calcified tissue or the ligand LI is an element selected from the group consisting of elements of atomic number 6-9, 15-17, 21-29, 31, 35, 37-44, 49, 50, 53, 56-70, 72-75, 81, 83 and 85.

32. The compound having affinity with a calcified tissue according to claim 31, wherein the metal atom is radioactive, paramagnetic or X-ray impermeable.

33. The compound having affinity with a calcified tissue according to any one of claims 1 to 30, wherein the metal atom or isotope element is a radioactive nuclide selected

from the group consisting of 11-C, 15-O, 18-F, 32-P, 59-Fe, 67-Cu, 67-Ga, 81-Rb, 89-Sr, 90-Y, 99m-Tc, 111-In, 123-I, 124-I, 125-I, 131-I, 117m-Sn, 153-Sm, 186-Re, 188-Re, 201-Tl, 211-At, 212-Bi and 213-Bi.

5 34. The compound having affinity with a calcified tissue according to any one of claims 1 to 30, wherein the metal atom or isotope element is an element selected from the group consisting of chromium (III), manganese (II), iron (II), iron (III), praseodymium (III), neodymium (III),
10 samarium (III), ytterbium (III), gadolinium (III), terbium(III), dysprosium (III), holmium (III), and erbium (III).

35. The compound having affinity with a calcified tissue according to any one of claims 1 to 30, wherein the metal
15 atom or isotope element is an element selected from the group consisting of bismuth, tungsten, tantalum, hafnium, lanthanum, lanthanide, barium, molybdenum, niobium, zirconium and strontium.

36. The compound having affinity with a calcified tissue
20 according to any one of claims 1 to 35, which is in a form of a salt, a hydrate, a solvate, an aggregate, an aqueous solution or a lyophilized product.

37. The compound having affinity with a calcified tissue according to any one of claims 1 to 36, wherein the
25 particle size is 1 nm to 50 μ m.

38. A composition for producing a complex compound having affinity with a calcified tissue, which comprises

a compound having affinity with a calcified tissue according to any one of claims 1 to 6 and 8 to 29, a peroxide ion of a transition metal, and a reducing agent.

39. A therapeutic agent which comprises a compound
5 having affinity with a calcified tissue according to any one of claims 1 to 37.

40. A pharmaceutical composition which comprises a compound having affinity with a calcified tissue according to any one of claims 1 to 37 or a salt thereof
10 and at least one pharmacologically acceptable carrier.

41. A kit for preparing a radioactive labeled compound, which comprises a compound having affinity with a calcified tissue according to any one of claims 1 to 37.

42. A diagnostic agent, imaging agent or therapeutic
15 agent, which comprises a compound having affinity with a calcified tissue according to any one of claims 1 to 37.

43. A radioactive labeled compound diagnostic agent, imaging agent or therapeutic agent, which comprises a compound having affinity with a calcified tissue
20 according to claim 33, a salt or an aggregate thereof.

44. A nuclear magnetic resonance imaging agent which comprises a compound having affinity with a calcified tissue according to claim 34, a salt or an aggregate thereof.

25 45. An X-ray imaging agent which comprises a compound having affinity with a calcified tissue according to claim 35, a salt or an aggregate thereof.

46. A method of selectively modifying an amino group at a terminal end, which comprises providing an amino oligosaccharide having 2 to 50 saccharide units which consists of one or more monosaccharides selected from the group consisting of glucosamine, mannosamine and galactosamine and is reduced at a terminal end thereof, and subjecting the amino oligosaccharide to a reaction for generating a carbamate compound.
47. A method of selectively modifying an amino group at a terminal end with a butoxycarbonyl (Boc) group, which comprises reacting, dibutyl dicarbonate, an aminosaccharide of 2 to 13 saccharide units which consists of one or more monosaccharides selected from the group consisting of glucosamine, mannosamine and galactosamine and reduced at a terminal end thereof.